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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
JOIKE, MICHELE K	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 09/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

TX

Office Action Summary	Application No.	Applicant(s)	
	10/686,199	BUDWORTH ET AL.	
	Examiner	Art Unit	
	Michele K. Joike, Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-10 and 12-19* is/are pending in the application.

4a) Of the above claim(s) *18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5-10 and 12-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of a reply to the previous Office Action, filed July 3, 2006. Amendments were made to claims 1, 9 and 16. Claims 4 and 11 were canceled. Claims 1-3, 5-10 and 12-19 are pending, claims 1-3, 5-10 and 12-17 are under consideration.

Any rejection of record in the previous Office Action, mailed March 8, 2006, that is not addressed in this action has been withdrawn.

Because this Office Action only maintains rejections set forth in the previous Office Action and/or sets forth new rejections that are necessitated by amendment, this Office Action is made FINAL.

Response to Arguments Concerning Claim Rejections – 35 USC § 102 (b) and 35 USC §103(a)

Applicants' arguments filed on July 3, 2006 have been fully considered. The following grounds of traversal are presented:

For the 102(b) rejection, Applicants argue that Cronan does not teach the newly added step of claims 1, 9 and 16 of identifying any binding partners that bind said protein of interest in said complex.

For the 103(a) rejections, Applicants argue that Cronan does not teach the newly added step of claims 1, 9 and 16 of identifying any binding partners that bind said protein of interest in said complex, and since Rigaut does not cure these deficiencies, there is no motivation to combine the references. Applicants also argue that neither Luo

nor Fields cures the deficiencies of Cronan or the lack of motivation to combine Cronan and Rigaut.

Applicant's traversal has been fully considered and found to be persuasive in that Cronan does not teach the newly added step of claims 1, 9 and 16 of identifying any binding partners that bind said protein of interest in said complex. However, applicants' amendment has necessitated the new grounds of rejection under 35 U.S.C. 103(a) recited below.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 9, 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cronan in view of Fields.

Applicants claim a method for obtaining *in vivo* binding partners of a protein comprising obtaining a cell and expressing a fusion protein comprising a protein of interest and a post-translational modification sequence; growing the cell under conditions to permit expression and modification; contacting the cell extract with an affinity purification reagent; and separating the complex from the extract. The fusion protein is a heterologous protein, and there is a cleavage site between the protein of interest and the post-translational sequence. The method also includes identifying

binding partners, including a plurality of binding partners. The method can also be performed by transforming a cell with a vector encoding the fusion protein.

Cronan (U.S. 5,252,466, specifically Summary of Invention, 1st, 4th and 5th paragraphs, Field of Invention, Detailed Description, p. 13 and 18, Examples 1 and 7, Claims 1, 2 and 7) teaches a method for obtaining *in vivo* binding partners of a protein comprising obtaining a transformed host cell (bacteria, yeast, other fungi, plant, insect or mammalian) and expressing a fusion protein comprising a protein of interest and a post-translation biotination sequence; growing the cell under conditions to permit expression and modification; contacting the cell extract with an affinity purification reagent; and separating complex from the extract. The fusion protein is a heterologous protein, and there is a cleavage site between the protein of interest and the post-translation biotination sequence. The method can also be performed by transforming a cell with a vector encoding the fusion protein. However, Cronan does not teach identifying any binding partners that bind said protein of interest in said complex.

Fields (U.S. 5,283,173, see entire document, specifically column 3, paragraph 2) teaches a yeast two-hybrid assay for identifying binding partners to a test protein, including using a library of cDNA plasmids.

The ordinary skilled artisan, desiring to perform the method described above with a plurality of nucleic acid expression vectors would have been motivated to combine the teachings of Cronan of obtaining a cell and expressing a fusion protein comprising a protein of interest and a post-translational modification sequence; growing the cell under conditions to permit expression and modification; contacting the cell extract with an

affinity purification reagent; and separating complex from the extract with Fields teaching a library of cDNA plasmids for use in a two-hybrid to identify protein interactions, because Fields teaches that an advantage of producing a multiplicity of proteins is that they can be simultaneously tested and detected for interaction. It would have been obvious to one of ordinary skill in the art to use a plurality of nucleic acid expression vectors because they can produce many binding partners and be used to test affinity reagents. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 1, 2, 5-9 and 12-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cronan in view Fields and in further view of Rigaut et al.

Applicants claim the method described above further limited by the fusion protein comprising an affinity purification sequence, wherein the purification sequence is a *S. aureus* protein A IgG binding domain or a calmodulin binding peptide and affinity purifying the protein of interest after the separating step.

Cronan (U.S. 5,252,466, specifically Summary of Invention, 1st, 4th and 5th paragraphs, Field of Invention, Detailed Description, p. 13 and 18, Examples 1 and 7, Claims 1, 2 and 7) and Fields (U.S. 5,283,173, see entire document, specifically column 3, paragraph 2) teach all of the limitations as described above. However, they do not teach affinity tagging the fusion protein, or cleaving the protein of interest from the post-translational modification sequence prior to identifying binding partners of the protein of

interest. Rigaut et al (Nature Biotech, 17: 1030-1032, 1999, see entire article, specifically Figure 1) teach a transformed yeast cell with a fusion protein comprising a heterologous protein with two affinity tags, a *S. aureus* protein A IgG binding domain and a calmodulin binding peptide, as well as a TEV cleavage site. They also teach making a cell extract and purification of the protein of interest. They also teach that the target protein is cleaved before purification and electrophoresis. Therefore, the target protein is cleaved from the post-translational modification sequence prior to identifying binding partners of the target protein.

The ordinary skilled artisan, desiring to perform a method for obtaining *in vivo* binding partners of a protein comprising obtaining a cell and expressing a fusion protein comprising a protein of interest and a post-translational modification sequence; growing the cell under conditions to permit expression and modification; contacting the cell extract with an affinity purification reagent; and separating complex from the extract with the fusion protein being a heterologous protein, and there is a cleavage site between the protein of interest and the post-translational sequence, and to use a fusion protein comprising an affinity purification sequence, wherein the purification sequence is a *S. aureus* protein A IgG binding domain or a calmodulin binding peptide and affinity purifying the protein of interest after the separating step, would have been motivated to combine the teachings of Cronan of obtaining a cell and expressing a fusion protein comprising a protein of interest and a post-translational modification sequence; growing the cell under conditions to permit expression and modification; contacting the cell extract with an affinity purification reagent; and separating complex from the extract and

Fields of identifying binding partners of a protein of interest with the teachings of Rigaut et al, of a fusion protein comprising an affinity purification sequence, wherein the purification sequence is a *S. aureus* protein A IgG binding domain or a calmodulin binding peptide and affinity purifying the protein of interest after the separating step. There would be motivation to combine the teachings because affinity tagging allows for rapid purification of proteins, especially heteromeric complexes. It would have been obvious to one of ordinary skill in the art to use affinity tagging for purification because these affinity tags do not impair function and allow for efficient recovery. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 1-3, 5-10 and 12-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cronan in view of Fields, in view of Rigaut et al, and in further view of Luo et al.

Applicants claim the method described above further limited by use of a mammalian host cell.

Cronan (U.S. 5,252,466, specifically Summary of Invention, 1st, 4th and 5th paragraphs, Field of Invention, Detailed Description, p. 13 and 18, Examples 1 and 7, Claims 1, 2 and 7), Fields (U.S. 5,283,173, see entire document, specifically column 3, paragraph 2) and Rigaut et al (Nature Biotech, 17: 1030-1032, 1999, see entire article, specifically Figure 1) teach all of the limitations as described above. However, they do

not teach the use of a mammalian host cell. Luo et al (U.S. 6,114,111, specifically Background, 4th paragraph) teach the use of a mammalian cell containing a fusion protein.

The ordinary skilled artisan, desiring to perform the method described above in mammalian cells would have been motivated to combine the teachings of would have been motivated to combine the teachings of Cronan of obtaining a cell and expressing a fusion protein comprising a protein of interest and a post-translational modification sequence; growing the cell under conditions to permit expression and modification; contacting the cell extract with an affinity purification reagent; and separating complex from the extract and Fields of identifying binding partners of a protein of interest with the teachings of Rigaut et al, of a fusion protein comprising an affinity purification sequence, wherein the purification sequence is a *S. aureus* protein A IgG binding domain or a calmodulin binding peptide and affinity purifying the protein of interest after the separating step and Luo et al of use of a mammalian cell containing a fusion protein. There would be motivation to combine the teachings because Cronan teaches that there are a large number of available and well-known host cells, including mammalian cells available to perform this method and Luo et al teach mammalian cells are desirable for fusion proteins because mammalian cells have different post-translational modification systems than yeast. It would have been obvious to one of ordinary skill in the art to use mammalian cells because they are they can be tested under a variety of experimental conditions that may affect intracellular protein-protein interactions. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of

the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Allowable Subject Matter

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele K. Joike, Ph.D. whose telephone number is 571-272-5915. The examiner can normally be reached on M-F, 9:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michele K Joike, Ph.D.
Examiner
Art Unit 1636

DAVID GUZO
PRIMARY EXAMINER